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211/26, 401/04

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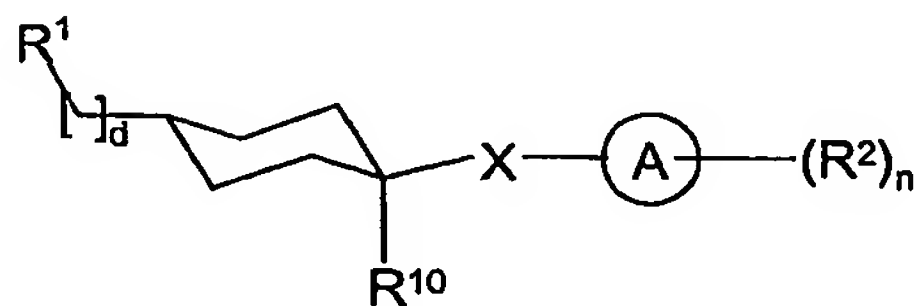
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(54) Title: CYCLOHEXYL COMPOUNDS AS CCR5 ANTAGONISTS



(57) Abstract: The present invention relates to compounds of formula (I), or pharmaceutically acceptable derivatives thereof, useful in the treatment of CCR5-related diseases and disorders, for example, useful in the inhibition of HIV replication, the prevention or treatment of an HIV infection, and in the treatment of the resulting acquired immune deficiency syndrome (AIDS).

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CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR,
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European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE,
SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG).

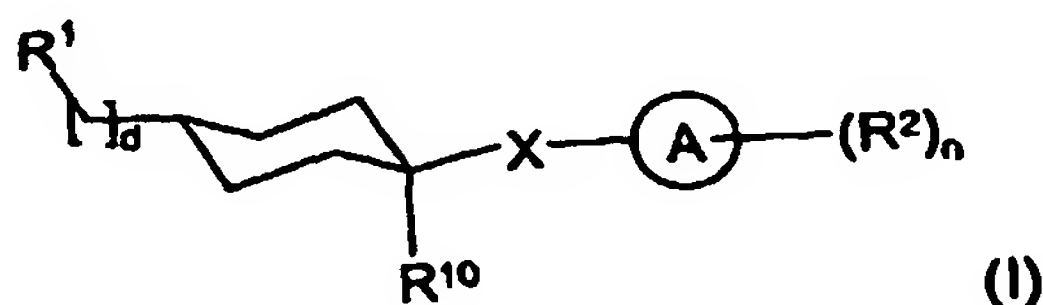
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ning of each regular issue of the PCT Gazette.*

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INTERNATIONAL SEARCH REPORT

Interr. application No
PC1, 03 03/39732

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/46 A61K31/438 A61P31/18 A61P31/04 C07D451/02
C07D471/10 C07D333/52 C07D211/26 C07D401/04
/(C07D471/10,235:00,221:00),(C07D471/10,221:00,209:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data, BEILSTEIN Data, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 182 195 A (TAKEDA CHEMICAL INDUSTRIES LTD) 27 February 2002 (2002-02-27) page 130, line 49 - line 51; claims 1,16; examples 70,73	1-21, 23-36
X	WO 01/72751 A (MUNSCHAUER RAINER ; BASF AG (DE); RAFFERTY PAUL (GB); JOHNSTON DAVID N) 4 October 2001 (2001-10-04) claim 1; examples 197,196	1-21, 23-39
E	EP 1 403 255 A (SUMITOMO PHARMA) 31 March 2004 (2004-03-31) claims; example 159	1-21, 23-39
X	US 6 479 487 B1 (BORCHERDING DAVID R ET AL) 12 November 2002 (2002-11-12) column 138, paragraph 5; claims; examples 29,18; table 1	1-21, 23-39
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

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Härtinger, S

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Inten I Application No

PCi/US 03/39732

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	WOLTERSDORF O W ET AL: "Topically Active Anhydrase Inhibitors. 1. O-Acyl Derivatives of 6-Hydroxybenzothiazole-2-sulfonamide" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 32, no. 11, 1989, pages 2486-2492, XP002282653 ISSN: 0022-2623 example 28; table 1 -----	1,4-7, 27,28, 33,34
X	WO 97/20823 A (CRISCIONE LEOLUCA ; YAMAGUCHI YASUCHIKA (CH); CIBA GEIGY AG (CH); MAH) 12 June 1997 (1997-06-12) claims 1-8; examples -----	1,4-7, 27,28, 33,34
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P,X	WO 03/087098 A (DAVIES DAVID THOMAS ; MARKWELL ROGER EDWARD (GB); BROOKS GERALD (GB);) 23 October 2003 (2003-10-23) claims 1-11; examples -----	1,4-7, 25,27, 28,31, 33,34
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P,X	WO 03/070244 A (ABBOTT LAB) 28 August 2003 (2003-08-28) page 40 - page 44; claims 1-36 -----	1,4-7, 27,28, 33,34
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INTERNATIONAL SEARCH REPORT

 Interna Application No
 PCT/JP 03/39732

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 03/075853 A (SQUIBB BRISTOL MYERS CO ; CHERNEY ROBERT J (US)) 18 September 2003 (2003-09-18) claim 26; example 122	1,4-7, 23-39
P,X	WO 03/028641 A (OMODERA KATSUNORI ; SEKIGUCHI YOSHINORI (JP); KANUMA KOSUKE (JP); TAIS) 10 April 2003 (2003-04-10) claims 1,13; examples	1,4-7, 27,28, 33,34
X	WITHERINGTON ET AL: "Conformationally restricted indolopiperidine derivatives as potent CCR2B receptor antagonists" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 11, no. 16, 2001, pages 2177-2180, XP002208447 ISSN: 0960-894X	1-6, 12-15, 17, 19-21, 23-39
A	table 5; compound 8	7-11,16, 18,22
E	EP 1 378 510 A (ONO PHARMACEUTICAL CO) 7 January 2004 (2004-01-07)	1-7,11, 16, 19-21, 23-39
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A	claims; example 10	7-22
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A	claims; example 4	7-22

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/39732

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1-21, 23-27, 33-39
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 23-27 and claims 37-39 are directed to a method of treatment of the human body, the search has been carried out and based on the alleged effects of the compound, however, only to the extent to which the compound could be searched.
2. ☒ Claims Nos.: 1-21, 33-36
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
1-39(part)
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 23-27 and claims 37-39 are directed to a method of treatment of the human body, the search has been carried out and based on the alleged effects of the compound, however, only to the extent to which the compound could be searched.

Continuation of Box I.2

Claims Nos.: 1-21,33-36

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. As the formula I basically amounts define a nitrogen containing group (cf. R1) substituted cyclohexyl ring, which is bound via a linker of one to 5 elements selected from carbon, nitrogen, oxygen, sulfur or phosphorus (cf. X) to a further nitrogen containing ring (cf. ring A), the substructure search in the STN Registry database resulted in more than 3400 compounds even for a refined search, which takes into consideration the further definitions in claim 1. So many documents were retrieved relating to the said compound hits, some of them also relate to the claimed antiviral and antibacterial use, that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claims is impossible. Consequently, the search has been restricted to the use of the said compounds in the treatment of viral or bacterial infections (cf. claims 23 and 25).

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internal Application No

PCT/US 03/39732

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INTERNATIONAL SEARCH REPORT

information on patent family members

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Application No

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